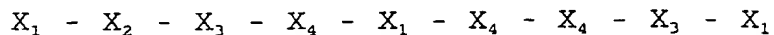


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Claims:

1. An isolated and purified peptide of the RY domain, having an amino acid sequence of general formula I:



X_1 = Phe, Tyr, or any amino acid having a substituted aromatic residue;

X_2 = Glu, Asp, Ser, or any amino acid having a $-(CH_2)_n-COO^-$ residue, wherein $n = 0-3$;

X_3 = Asp, Thr, any aliphatic amino acid, or any of amino acids X_4 ; and

X_4 = Arg, Lys, or any amino acid having a $-(CH_2)_n-NH_3^+$ residue, or a $-(CH_2)_n-NH-C(NH_3^+)NH_2$ residue wherein $n =$

0-4;

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as well as functional equivalents thereof.

2. A peptide according to Claim 1, wherein Methionine (Met) is connected to the N-terminal of the sequence of general formula I.
3. A peptide according to Claim 1 or 2 wherein in the sequence of general formula I, the sequence is $X_4 - X_1 - X_4 - X_4$ stands for Arg - Tyr - Arg - Arg.
4. A peptide according to Claim 3, wherein the sequence is preceded by $X_3 = \text{Arg}$.
5. A peptide according to ^{Claim 1} ~~any of Claims 1 to 4~~, wherein the substituted aromatic residue of X_1 is Phenyl- $(CH_2)_n$ -.
6. A peptide according to ^{Claim 1} ~~any of Claims 1 to 5~~, wherein the aliphatic amino acid of X_3 is selected among Leu, Ile, Ala, Gly and Val.
7. A death inhibitory peptide, DIP1, having the following amino acid sequence: Phe-Glu-Leu-Arg-Tyr-Arg-Arg-Ala-Phe. 1
8. A death inhibitory peptide, DIP2, having the following amino acid sequence: Phe-Ser-Arg-Arg-Tyr-Arg-Arg-Asp-Phe. 2
9. A death inhibitory peptide, DIP2, having the following amino acid sequence: Phe-Glu-Thr-Arg-Phe-Arg-Arg-Thr-Phe. 3
10. A pharmaceutical composition comprising as active ingredient a DIP according to ^{Claim 1} ~~any of Claims 1 to 9~~ or a functional equivalent thereof.
11. A pharmaceutical composition according to Claim 10 comprising a pharmaceutical acceptable carrier.

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12. The use of the DIP or of a pharmaceutical composition
according to ^{Claim 1} ~~any of Claims 1 to 11~~ in the preparation of a

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medicament.

a 13. A method for the treatment of disorders of inappropriate activation of apoptosis by a DIP or by a pharmaceutical composition according to ~~any of Claims 1 to 11~~. *Claim 1*

a 14. A method for increasing the number of viable cells in a biological tissue by a DIP or by a pharmaceutical composition according to ~~any of Claims 1 to 11~~. *Claim 1*

15. A method for the enhancement for the survival of biological cells by a DIP or by a pharmaceutical composition according to any of Claims 1 to 11.

16. A method for the preparation of a DIP of general formula I according to Claim 1, which comprises attaching the corresponding amino acids, one after the other, onto a functionalized resin, by the following steps:

- a. synthesising the sequence of Fmoc (9-fluorenyl methoxycarbonyl)-N^{alpha}-protected amino acids activated in situ in a suitable synthesizer and coupling same to a preloaded resin, removing the protecting group and repeating the coupling and deprotecting steps until the entire peptide synthesis has been finalized;
- b. cleaving the peptide from the resin,; and
- c. purifying the peptide obtained in step b.

17. A method according to Claim 16, wherein the synthesizing step is performed by using an ABI (Applied Biosystems U.K.) 433 A synthesizer.

18. A method according to Claim 16 or 17, wherein the coupling reagent is HBTU/HOBt (benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate/N-hydroxybenzotriazole).

a 19. A method according to ~~any of Claims 16 to 18~~, wherein 3 equivalents of each of the activated amino acids is used in each coupling step. *Claim 16*

a 20. A method according to ~~any of Claims 16 to 19~~, wherein the resin is selected among a Wang resin and a 2-chlorotrityl resin. *Claim 16*

a 21. An isolated and purified peptide of the RY domain having an amino acid sequence of general formula I as defined in ~~Claim 1 or 2~~ *Claims 1 and 2*, substantially as herein described with reference to the examples. *Claims 5*

22. An in vitro assay system for the regulation of cell death by an isolated and purified peptide of the RY domain according to any of Claims 1 to 9, which comprises:
- a. transient transfection of cultured cells via electroporation or cationic-lipid mediated transfection by an expression vector, harboring a reporter gene;
 - b. co-transfecting the reporter gene with a second expression vector, carrying either the death inhibitor or the death inducer genes, thus affecting the cellular apoptotic threshold towards life or death, respectively;
 - c. performing transfection of cells with a combination of both the death inhibitor and the death inducer genes to examine the activity of each of these two proteins in opposing the death-inhibitory or promoting-effect of the other, respectively;
 - d. testing the effects of the peptides as potential modulators of the activity of the Bcl-2 system, by testing each peptide by one of the following two modes of administration into the cells:
 - e. 1. small, membrane permeable peptide particles are administered by addition to the extracellular medium;
 2. cell membrane-impermeable small peptide particles are administered by electroporation or by liposome-mediated transfection;
 - f. evaluating the potential of the peptides to inhibit cell death by measuring their ability to overcome bax-induced death process; and
 - g. assessing the potential of the peptides to trigger apoptosis by measuring their ability to induce death by themselves, their activity in counteracting Bcl-2 activity, and /or their effect in augmenting Bax cellular toxicity.
23. An in vitro assay according to Claim 22, wherein the peptide is tested in addition by constructing small peptides into expression vectors which contain DNA sequences, encoding for the desired peptide; said peptide being transfected into cells via electroporation or cationic-lipid-mediated

transfection.

24. An in vitro assay system as defined in Claim 22, substantially as described in Example 3.b.3.